Amendments to the Specification:

On page 3, the 3rd paragraph, beginning on line 20, is amended to read as follows:

U.S. Pat. No. ~~5,736,35~~ 5,736,354, issued to Fielden, et al., discloses a method of determining the toxicity of a fluid sample comprising mixing the sample with a suspension of light emitting organisms; monitoring the light output of the mixture continually over a period of time; and providing an assessment of toxicity based on changes in light transmission.

On page 10, the 3rd paragraph, beginning on line 14, is amended to read as follows:

It will be appreciated that in such a modeling, there ~~eam~~ can be a number of different types of markers, including general markers, group markers (for example, cholestasis, necrosis, stenosis), and compound specific markers.

On page 10, the 4th paragraph, beginning on line 17, is amended to read as follows:

It will appreciated that there are preferred model attributes. These include: time stability (must be able to predict toxicity over an extended time range); dose dependency (should only score toxic doses of compounds); vehicle independence (should not be sensitive to type of vehicle used); predictable (based on statistical inference with known false positive rate); and powerful (false negative rates should be low enough that ~~singeltons~~ singletons or low number of replicates can adequately predict toxicity).

On page 11, the 1st paragraph, beginning on line 1, is amended to read as follows:

In another preferred embodiment of the present invention, there are various stages of model development. These, preferably, include: selection (determination of relevant expression patterns that are time stable and dose dependent); quantification (production of composite measures that define patterns); prediction (use of composite measures to assign probability of patterns being the same); and validation (ability to provide statistical measures of model accuracy).

On page 12 the 1st paragraph, beginning on line 3, is amended to read as follows:

The ability to tell whether a chemical compound has a high probability of being toxic based on its gene expression profile. ~~This~~ is a critical issue for the safety of potential pharmaceutical compounds

On page 24, the 1st paragraph, beginning on line 1, is amended to read as follows:

The phrase "hybridizing specifically to", refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent conditions when that sequence is present in a complex mixture (e.g., total cellular) DNA or RNA. The term "stringent conditions" refers to conditions under which a probe will hybridize to its target subsequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. Generally, stringent conditions are selected to be about 5° C[[.]] lower than the thermal melting point (Tm) for the specific sequence at a defined ionic strength and pH. The Tm is the temperature (under defined ionic strength, pH, and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. (As the target sequences are generally present in excess, at Tm, 50% of the probes are occupied at equilibrium). Typically, stringent conditions will be those in which the salt concentration is at least about 0.01 to 1.0 M Na ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30° C[[.]] for short probes (e.g., 10 to 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide.

On page 31, the 2nd paragraph, beginning at line 9, is amended to read as follows:

The classification of objects into one or more groups based on many measurements has several well established techniques. These include discriminate analysis, logistic regression, multidimensional scaling, clustering, and neural networks. A general discussion of each technique can be found in "Multivariate Analysis, Prentice Hall ISBN 0-13-894858," which is incorporated herein by reference. All of these methods work by making

composite measures from the many measurements taken from each object. With gene expression patterns we have several time and dose points which represent multiple objects that are grouped together. None of these techniques ~~are~~ is sufficient alone to represent this order of complexity. Contrast analysis allows us to identify measurements that are ~~partial~~ partially independent of time because they are time stable yet are affected by toxic doses more then ~~non-toxic~~ non-toxic doses. The PCA combines these many measurements into a series of orthogonal composite measures. Since these composite measures are ~~non correlated~~ non-correlated by definition, the problem of ~~multicolinearity~~, multi-colinearity, which can decrease the power of logistic regression, is eliminated. By combining these techniques in the order described, many of the limitations of each individual technique is reduced.

On page 33, the 6th paragraph, beginning at line 21, is amended to read as follows:

The invention consists of three distinct stages. At each stage, small variations in technique can be used to accomplish the same task. The first stage, selection of time stable and dose dependent patterns by contrast analysis, can be altered by changing the method of measuring variation. We use a method that is based on analysis of variance, where the time component and dose component are assessed simultaneously. One could use a series of t test on individual parts of the pattern to get a collective set of p values that could approximate our method of measuring variation. One could also set an arbitrary fractional cutoff, mean or median of experimental group divided by control group, to approximate the measurement of variation for each part of the pattern that is then ~~use~~ used in the next ~~to~~ two stages of analysis. The novel feature is to find time[[.]] stable and dose dependent patterns with a predicted p value for that pattern.